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| 13. SUPPLEMENTARY NOTES                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |                        |                                          |                                                   |                                            |
| 14. ABSTRACT- Purpose: Determine whether military employment is associated with the risk of developing Parkinson's disease (PD). Scope: Two large population-based case-control studies of PD that were carried out in a health maintenance organization. Major findings: When compared to the men who had never served in the military, men that served in the military during peacetime but never during a conflict were not at increased risk of PD. However, the risk of PD was significantly increased among men who were deployed during one or more wars (adjusted OR= 1.8, 95% CI 1.2-2.8; p<0.01). The risk of PD was increased among men who were deployed during World II (OR = 2.1, 95% CI 1.3-3.6, p<0.005) or Viet Nam (OR = 2.6, 95% CI 0.9-7.13, p<0.07), but not among men who served during those time periods who were not deployed. No increased risk of PD was observed among men who were in the military at the time of the Korean conflict, either among the deployed or the non-deployed. Significance: Identifying the military occupations and exposures that are associated with a higher risk of PD could lead to important etiologic clues to this disabling neurodegenerative disease. |                  |                        |                                          |                                                   |                                            |
| 15. SUBJECT TERMS<br>Uæ\ ä • [ ] q Åä^æ^LÄ^~   [ ä^*^ } ^ ææ^ Åä^æ^LÄ äææ^ Ä^ çæ^LÄ^   [ ^ { ^ } dÄä \LÄ] æ^ { ä   [ * äÄ ç ä^Lææ^Æ } d [  Ä ç ä^                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                  |                        |                                          |                                                   |                                            |
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## 1. INTRODUCTION:

The primary objective of this project was to determine whether military service is associated with the risk of developing Parkinson's disease (PD). We examined the association between military service and the risk of developing PD using data from two recently completed community-based case-control studies of PD conducted in the Kaiser Permanente Northern California (KPNC) health maintenance organization. The overall study included 496 incident (newly diagnosed) patients with PD and 541 population controls. Because military service was rare among women, the investigation of military employment was restricted to 300 male patients and 329 control men without PD. We constructed measures of military occupational and deployment exposure using objective data from each subject's structured interview, which includes extensive information on lifetime occupational and residential history, as well as military job titles and war-zone deployment data. We also constructed variables to control for potential confounding factors that could influence the association between military employment and PD (cigarette smoking, caffeine consumption, alcohol intake, sociodemographic characteristics). Our statistician analyzed the data using multivariate unconditional logistic regression, with adjustment for age and other potential confounding variables.

## 2. KEYWORDS: Provide a brief list of keywords (limit to 20 words).

Parkinson's disease; neurodegenerative disease; military service; deployment; epidemiologic study; case-control study

## 3. OVERALL PROJECT SUMMARY:

### Methodology

Our biostatistician performed extensive data cleaning procedures and quality control measures on all of the study data, as well as logical cross-checks of variables to identify discrepant data. She constructed all of the variables that were examined in statistical analyses as potential confounding factors that could influence the association between military employment and PD. The preliminary data management steps also required extensive coding of military jobs, as well as statistical analyses of data on lifetime occupational and residential history, military service and deployment, and locations of service. For risk analyses, our comparison group was comprised of men who did not serve in the military, and we examined the risk of PD among those who served during periods of conflict, as well as with those who served only during peacetime or during times of conflict but in stateside military occupations. In the last months of the project, we carried out analyses that adjusted for other risk factors (i.e., confounders) that could in part explain the association between military employment and PD. Potential confounding variables included measures of tobacco exposure (cigarette, cigar and pipe smoking; duration and quantity of tobacco exposure; pack-years of smoking), caffeine intake (frequency and quantity of consumption), alcohol exposure (type of alcohol exposure, frequency and quantity of consumption), demographic variables (education, socioeconomic status, income) and other important covariates.

## Summary of Results, Progress and Accomplishments

The frequency of military service was very high among men who were on average age 70 in 1994-95; 69% of men with Parkinson's disease and 64% of their age-matched controls had served in the military. When compared to the men who had never served in the military or to men who served in the military but not at times of war, men who were veterans of war had a two-fold increased risk of Parkinson's disease. When compared to the men who had never served in the military, men that served in the military during peacetime but never during a conflict, were not at increased risk of PD (adjusted odds ratio (OR) = 1.1, 95% confidence interval (CI) 0.7-1.5; p-NS). However, the risk of PD was significantly increased among men who were deployed during one or more wars (adjusted OR= 1.8, 95% CI 1.2-2.8; p<0.01).

Interestingly, the risk of PD was increased among men who were deployed during World II (OR = 2.0, 95% CI 1.2-3.3, p<0.005), but not among men who served at the time of World War II who were not deployed) (OR = 1.0, 95% CI 0.7-1.6; p-NS). Similarly, the risk of PD was increased among men who were deployed during the Vietnam war (OR = 2.3, 95% CI 0.9-6.2, p<0.10), but not among men who served at the time of the Vietnam war but were not deployed (OR = 1.0, 95% CI 0.5-1.7; p-NS). No increased risk of PD was observed among men who were in the military at the time of the Korean war, either among the deployed (OR = 1.7, 95% CI 0.9-3.2, p-NS) or the non-deployed (OR = 1.2, 95% CI 0.7-2.1; p-NS).

Of note is that the associations between military deployment during wars and PD were not affected after statistical adjustment for known factors associated with PD, including cigarette smoking, caffeine consumption, alcohol intake, education or socioeconomic status.

## 4. KEY RESEARCH ACCOMPLISHMENTS:

- A sizable proportion (> 40%) of U.S. men who are currently at the age of risk for developing Parkinson's disease have been deployed in previous U.S. military conflicts or have been employed by the military during peacetime, making it important to investigate a possible association of military service and PD in this aging cohort.
- When compared to the men who had never served in the military, men who were veterans of war had a 1.8-fold increased risk of Parkinson's disease. In contrast, employment in the military that did not involve deployment during wartime was not associated with an increased risk of PD.
- Deployment during World War II was associated with a doubling of PD risk, and deployment during Viet Nam War was associated with a 2.3-fold increased risk of PD. Deployment at the time of the Korean war was not associated with an increased risk of PD.
- These findings raise concerns that physical or chemical exposures during wartime military service affect the risk of developing Parkinson's disease later in life. Given that a sizable proportion (> 40%) of U.S. men who are currently at the age for developing PD have been deployed during previous U.S. military conflicts, the potential public health significance is tremendous.
- Additional studies using more extensive retrospective exposure assessment are needed to investigate physical, infectious and/or chemical exposures that could explain the increased risk of PD among men who were previously deployed during wartime.

## 5. CONCLUSION:

The strengths of the project included the availability of a large group of well-characterized men with Parkinson's disease and age-matched controls from the same underlying population, which is racially diverse and broadly representative of the underlying population in the San Francisco Bay area. Moreover, the availability of life- long occupational and residential histories for all men in this study, as well as extensive information on other risk factors for PD, enabled a very efficient and cost-effective opportunity to examine the association of military service with Parkinson's disease. We are grateful to Department of Defense for recognizing this opportunity and for providing the support to carry out this project.

The results of our study raises concerns that physical or chemical exposures during wartime military service could affect the risk of developing Parkinson's disease. As is true for any single scientific study, the results of this study by themselves are not definitive, and replication of findings from this work will be very important. Because of the significant associations observed with deployment during the World War II and Viet Nam wars, we will pursue detailed objective information on the veterans in these studies, using data from the National Personnel Records Center (NPRC) in Saint Louis. These data will include information on branch of service, dates of service, place of discharge, reason for separation, military occupational code (MOC) specialty, military education, duty station(s) and assignment(s), ranks, military honors (decorations, medals, badges), and casualty records. We hope that validation of self-reported military service histories and the additional objective information on features of military deployment will add provide more rigor and more detail regarding the specific exposures that might explain the associations of PD with wartime deployment. Identifying the military occupations and exposures that are associated with a higher risk of PD will provide important clues to their etiology and could provide opportunities for future interventions to prevent or treat Parkinson's disease.

## 6. PUBLICATIONS, ABSTRACTS, AND PRESENTATIONS:

- a. We are in the process of preparing a manuscript describing the study results for submission to the journal *Neurology* (the top neurology journal).
- b. Nothing to report.

## 7. INVENTIONS, PATENTS AND LICENSES: List all inventions made and patents and licenses applied for and/or issued. Each entry shall include the inventor(s), invention title, patent application number, filing date, patent number if issued, patent issued date, national, or international.

**Nothing to report.**

## 8. REPORTABLE OUTCOMES: Provide a list of reportable outcomes that have resulted from this research. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. This list may include development of prototypes, computer programs and/or software (such as databases and animal models, etc.) or similar products that may be commercialized.

**Nothing to report.**

## **9. OTHER ACHIEVEMENTS:**

**Nothing to report.**

## **10. REFERENCES:**

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## **11. APPENDICES:**

**Nothing to report.**